PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Chia-Gee **WANG**
Serial No.: 10/651,305 Group No.: 1614
Filed: August 28, 2003 Examiner: Gregg Polansky
Confirmation No.: 9020
For: RADIOTHERAPY METHOD USING X-RAYS

Attorney Docket No.: **U 014775-5**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO OFFICIAL ACTION

The official action of 18 August 2009 has been carefully considered and reconsideration of the application in view of the present submission is respectfully requested.

CERTIFICATE OF MAILING/TRANSMISSION (37 CFR 1.8a)

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CLIFFORD J. MASS
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The claims stand rejected under 35 USC 103(a) as allegedly being unpatentable over Mills in view of Wang. Applicant respectfully traverses this rejection.

The claimed invention is based at least in part upon Applicant's discovery that, with the use of bright x-ray beams of defined line emissions tuned to the absorption edge of a selected element (e.g., platinum) in a compound associated with malfunctioning cells, it is possible to cause the emission of Auger electrons from the selected element associated with DNA of irradiated cells in a dose of at least 10^6 Gy *in situ* within a few atomic distances from the selected element. This causes the disruption of the DNA and death of the cells, while localizing the damage to such cells (specification at, e.g., paragraphs [0009], [0023] and [0029]). The sphere of damage is so localized (a few atomic distances) that it would be harmless everywhere in a cell except the DNA of the cell such that the Auger cascade can be used to destroy malfunctioning cells without destroying other cells outside of a very small ionization sphere.

In accordance with this discovery, all claims of record recite a step of irradiating a selected region, in which malfunctioning cells comprising a compound with the selected element associated with DNA of the malfunctioning cells are located, with line emission x-rays so as to cause emission of Auger electrons in a dose of at least 10^6 Gy *in situ* within a few atomic distances from the selected element whereby to localize the effects of disrupting DNA to the malfunctioning cells. As next discussed, this feature of the claimed method was not predictable to one of ordinary skill in the art

from the cited references and the references could not provide even a reasonable expectation of success for the invention as claimed.

The rationale for the rejection is provided in the paragraph bridging pages 4-5 of the official action as follows: "Therefore, one skilled in the art would have understood that the substitution of one monochromatic x-ray source (with distinct and specific frequency and energy level properties) for another source (with the same energy properties) would produce and achieve the same results (causing a Auger electron cascade from the platinum in the cisplatin) in the absence of evidence to the contrary". This rationale requires that the results of the substitution be **predictable**. See MPEP 2143 ("Exemplary Rationales that may support a conclusion of obviousness include . . . (B) Simple substitution of one known element for another to obtain **predictable** results. . . .").

One of ordinary skill in the art could **not** have predicted from the cited art that the substitution of the claimed line emission X-rays for the gamma-rays of Mills would produce and achieve the claimed results. To the contrary, Mills teaches that the effects described therein are obtained by "a radiation source which provides **energy at the corresponding resonant Mossbauer absorption frequency** of isotope containing pharmaceutical" (emphasis added). Mills at Abstract; see, also, column 2, lines 45 -50 ("The excitation is by a radiation source, the apparatus of the invention, at the corresponding resonant Mossbauer absorption frequency of selected tissue having received the administered pharmaceutical where excitation effects nuclear transitions to cause selective energy absorption in the selected target tissue."), and column 5, lines 7-13 ("Therefore, treatment is carried out by irradiating the selected tissue with gamma radiation of the proper energy and polarization and gamma ray propagation direction to match the conditions for resonant absorption by the Mossbauer absorber isotope atoms

of the pharmaceutical molecules present in the target selected tissue."). There is nothing in Mills that would show or suggest if or how the method described therein could be modified to create an Auger cascade other than by Mossbauer absorption using gamma rays of a corresponding Mossbauer absorption frequency. Moreover, the process described in Mills cannot be modified in the manner suggested by the Examiner in any event as this would improperly change the principle of operation of the reference. See MPEP 2143.01(VI) ("If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.").

In addition to the above, Applicant respectfully submits that there would not have been even a reasonable expectation of success with the claimed method since one of ordinary skill in the art would have expected that the use of X-rays to generate the claimed dose of 10^6 Gy *in situ* would result in unacceptable damage to a patient. Thus, although Cash et al US Patent 6,366,801 describes radiosurgery with the use of a heavy element contrast agent in connection with a monochromatic x-ray source with distinct and specific frequency and energy level properties (see Cash at column 8, line 46 to column 9, line 39 ("Optimized X-ray Spectrum")), Cash teaches that it is necessary to limit the radiation to a dose that is orders of magnitude less than the claimed dosage of 10^6 Gy *in situ*. See Cash et al at, e.g., column 12, lines 43-48 ("a preferred approach is to irradiate the patient 10 so that the tumor receives 1600 cGy in a single dose, and the surrounding healthy tissue receives 1600/de cGy."); see, also,

Cash at column 15, Example 1 ("At the skin, a dose of 10 Gy accumulates, which is **too high for healthy skin**." Emphasis added.). In other words, the art does not provide even a **reasonable expectation of success** that the claimed dosage could be used to provide for the preferential destruction of tumor cells in a subject while localizing the damage so as not to severely injure a patient. In the absence of such reasonable expectation of success, the cited art is incompetent to set forth even a *prima facie* case of obviousness for the invention as claimed. See MPEP 2143.02.

The Examiner has dismissed the Cash teaching of the limit on X-ray dosage with the statement that "Cash teaches methods which differ from those of Mills" (official action at page 7). Applicant respectfully submits that the claimed method differs from those described in Mills for the same reasons (as well as for the reasons discussed above).

The secondary reference cited by the Examiner cannot supplement the deficiencies in the primary reference even assuming for the sake of argument that the references were properly combinable. In particular, Wang does not show or suggest the use of line emission x-rays tuned to the K- or L- absorption edge of a select element to create an Auger cascade or that the same can be used selectively to destroy tumor cells **without destroying healthy tissue**.

In view of the above, Applicants respectfully submit that the prior art rejection and all other rejections and objections of record have been overcome and that

the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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